

Response to “Comment on ‘Insulin-like Growth Factor 1 – A Novel Biomarker of Abdominal Aortic Aneurysm’”

Mr. Koole and his prominent co-authors are thanked for their interest in our work and the kind words. This Viborg cohorte has demonstrated many significant and insignificant associations, so the risk of some chance findings is obvious. Mr. Koole et al. propose to add diabetes mellitus and use of glucocorticoids in the adjusting multivariate analysis. However, use of glucocorticoids is already included, and there were not many with diagnosed diabetics ($N = 7$). Consequently, IgF remained unchanged and significantly associated with growth rate. We have no variables concerning physical stress, and we did not measure HbA1c or hsCRP.

The authors further suggest combining IGF-1 and growth rate to analyse the additive value of using IgF1 instead of only AAA growth rate to predict need for later surgery. If to be used for such clinical purposes, growth rate is not optimal as it need longer observation time. Baseline AAA diameter is more relevant (Initial AAA max diameter AUC = 0.85, 95% C.I.: 0.77; 0.93), vs (IgF1 and AAA max diameter combined model: AUC = 0.87, 95% C.I.: 0.79; 0.94). Consequently, S-IgF1 doesn't seem to hold the potential for a clinical useful biomarker, only as a pathophysiological biomarker.

Finally, the authors ask about the numbers and power of cardiovascular events and all cause deaths. The number of cardiovascular

ischemic events ($N = 29$ (25%)) and deaths ($N = 37$ (32%)) was lower than later repairs ($N = 45$), and thus had a lower power. In addition, these two secondary variables are heterogeneous as all cause deaths also includes non-cardiovascular deaths and cardiovascular events included a number of various hospital discharge diagnoses due to ischemic events in the brain, heart and legs. They were not used as a composite endpoint, but separately. Nevertheless, the results concerning overall death and cardiovascular events may easily be due to misclassification bias and/or type 2 errors.

On behalf of my coauthors

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